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| 09/605,783 | 06/27/2000 | Jiangchun Xu | 210121.427C16 | 4968 |

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| EXAMINER | |
|---|---|
| JOHANNSEN, DIANA B | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1634 | |

DATE MAILED: 02/23/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/605,783 | XU ET AL. | |
| | Examiner | Art Unit | |
| | Diana B. Johannsen | 1634 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *09 January 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *35,36 and 62-66* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *35,36 and 62-66* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *20 December 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## FINAL ACTION

### *Continued Examination Under 37 CFR 1.114*

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 09 January 2006 has been entered.

2. All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

3. Claims 35-36 and 62-66 are pending and under consideration. Applicants' amendments and arguments have been thoroughly reviewed, but are not persuasive for the reasons that follow. Any rejections not reiterated in this action have been withdrawn.

4. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

***Specification***

5. It is noted that the new title of the application has now been entered.

***Claim Rejections - 35 USC § 112***

6. Claims 35-36 and 62-66 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods for stimulating and/or expanding "T cells" using a peptide encoded by a particular subsequence of SEQ ID NO: 110 (the peptide disclosed as SEQ ID NO: 337)(as well as for isolated T cell populations comprising T cells prepared by such methods), and for methods of stimulating and/or expanding P501S-specific T cells using fragments of SEQ ID NO: 110 comprising SEQ ID NO: 337 (as well as for isolated T cell populations comprising T cells prepared by such methods), does not reasonably provide enablement for methods for stimulating and/or expanding "T cells" (as recited in the claims) using the numerous other polypeptides encompassed by the claims, or for isolated T cell populations comprising T cells prepared by such methods. The specification does not enable any

person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to: (A) the breadth of the claims; (B) the nature of the invention; (C) the state of the prior art; (D) the level of one of ordinary skill; (E) the level of predictability in the art; (F) the amount of direction provided by the inventor; (G) the existence of working examples; and (H) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) (*MPEP* 2164.01(a)).

The claims as written encompass methods "for stimulating and/or expanding T cells specific for an amino acid sequence encoded by SEQ ID NO: 110," as well as isolated T cells prepared by the claimed methods. In the method of claim 35 and claims dependent therefrom, T cells are contacted with "a polypeptide comprising at least a 9 amino acid fragment of the amino acid sequence encoded by SEQ ID NO: 110," while dependent claim 62 further requires a polypeptide comprising one of six particular fragments encoded by SEQ ID NO: 110. In the method of claim 63 and claims dependent therefrom, T cells are contacted with "at least one antigen presenting cell that expresses or is pulsed with a polypeptide comprising at least a 9 amino acid fragment of the amino acid sequence encoded by SEQ ID NO: 110," while dependent claim 65 further requires that said polypeptide comprise one of six particular fragments

encoded by SEQ ID NO: 110. Finally, claim 66 is drawn to a method in which T cells are contacted with "at least one antigen presenting cell that expresses or is pulsed with a polypeptide comprising at least a 9 amino acid fragment of the amino acid sequence encoded by SEQ ID NO: 110," wherein the fragment "comprises the amino acid sequence of SEQ ID NO: 337."

It is again noted that SEQ ID NO: 110 and the predicted amino acid sequence encoded thereby, SEQ ID NO: 113, were first disclosed in parent application 09/020,956, filed February 9, 1998. It is also noted again that while the specification states that SEQ ID NO: 110 is expressed in both prostate tumor tissue and normal prostate tissue (see, e.g., pages 129-130 and 177), the specification provides evidence that detection of SEQ ID NO: 110 expression in cells obtained from patient blood samples would be one factor that one of skill in the art would reasonably consider in diagnosing prostate cancer, as such expression was evident in 6 of 8 samples from prostate cancer patients, and absent in 4 of 4 samples from normal blood samples (see pages 189-190 of the specification).

As discussed in the prior Office actions of 20 September 2004 and 08 July 2005, it is unpredictable as to whether one of skill in the art could make and use the invention in a manner reasonably commensurate with the claims. It is first noted that the specification discloses that a database search for sequences homologous to the polypeptide encoded by SEQ ID NO: 110 did not reveal any significant homologies (page 125); accordingly, the specification does not provide evidence, e.g., that SEQ ID NO: 110 or any polypeptide encoded thereby is homologous to a prior art molecule that

is known to encode or contain epitopes that stimulate T cells. The specification exemplifies only a single peptide contained within SEQ ID NO: 113 (and encoded by SEQ ID NO: 110) that stimulates naïve T cells (see the discussion of SEQ ID NO: 337 at pages 144-145 of the specification). In contrast, the instant claims as written encompass the use of thousands of different peptides and polypeptides in stimulation/expansion of any type of T cells. It is noted that the specification does exemplify the use of several subfragments of SEQ ID NO: 113 in stimulating P501S-specific T cells (Example 12); thus, one of skill in the art would reasonably expect that such subfragments comprising SEQ ID NO: 337 (as set forth in, e.g., claims 62, 65 and 66) would be useful in expansion of one specific type of T cell (those previously prepared using SEQ ID NO: 337, i.e., the P501S-specific cells of the specification). However, the instant claims are clearly not drawn to or limited to such cells – the claims as written merely require the use of "T cells." The P501S-specific T cells of the specification possess particular properties that predispose them to react with peptides and polypeptides comprising SEQ ID NO: 337, and are clearly not representative of all "T cells." Given the teachings of the specification, it is unknown as to whether any molecules encompassed by the claims (other than SEQ ID NO: 337) actually have the functional property of stimulating T cells of any type other than that employed in Applicants' example. Lacking guidance from the specification, one of skill in the art may look to the teachings of the art for further direction and enablement of a claimed invention. In the instant case, the prior art reference of Billing-Medel et al (U.S. Patent No. 6,130,043) does disclose a prostate-specific polypeptide sharing regions of identity

with instant SEQ ID NO: 113 for which basis is provided in Billing-Medel et al's priority application 08/850,713. However, Billing-Medel et al provide no evidence that this region or portions thereof have the ability to stimulate T cells; accordingly, the Billing-Medel et al reference does not support the enablement of the invention of the instant claims. Further, the prior art reference of Bixler et al (U.S. Patent No. 5,785,973 [7/1998; filed 6/1995]) teaches that while some general characteristics of T cell determinants are known (e.g., typical lengths), there are conflicting theories in the art with regard to what features or properties cause a particular peptide to actually function as a T cell determinant (see the section entitled "T-Cell Determinants" at columns 5-7, and particularly the conclusion at column 7, lines 36-37 that "A clear picture of what factors are important to the prediction of a T-cell determinant is yet to emerge"). Thus, the teachings of the prior art indicate that only certain, particular polypeptide fragments function as T cell determinants, and further that the guidance provided in the art at the time the instant invention was made was not sufficient to allow one of skill to predict which peptides encompassed by the instant claims -- if any --other than SEQ ID NO: 337 will actually stimulate "T cells" (as recited in the claims). While one of skill in the art could conduct further experimentation aimed at determining which of the thousands of molecules encompassed by the claims function as T cell determinants, the outcome of such experimentation cannot be predicted, and it is therefore unknown as to whether any molecules other than SEQ ID NO: 337 could actually perform this function. Further, the claims as written are clearly not limited to P501S-specific T cells such as those exemplified in, e.g., Example 12 of the specification. Accordingly, given the lack of

guidance in the specification and in the art, and the unpredictability of the art, it would require undue experimentation to make and use Applicants' invention in a manner reasonably commensurate in scope with the instant claims.

With regard to the rejection of claims 35-36 and 62-66 under 35 U.S.C. 112, first paragraph set forth in the prior Office action of 08 July 2005, the response traverses the rejection on the following grounds, which were not found to be persuasive for the reasons set forth below.

The response asserts that "Applicants' specification as filed describes numerous fragments of the polypeptide encoded by SEQ ID NO: 110 (referred to as P501S) that have been experimentally determined to be capable of stimulating T cells." The response first refers to Example 6, noting that it "demonstrates the identification of a naturally processed P501S epitope (SEQ ID NO: 337) that is expressed in the context of the human HLA-A2.1 molecule." In response, it is again acknowledged that the specification enables the use of the peptide of SEQ ID NO: 337 in stimulating and/or expanding T cells. The examiner has not disputed the enablement of this particular peptide; rather, the instant rejection pertains to the many other peptides and polypeptides encompassed by the instant claims.

The response next refers repeatedly to Example 12, arguing that the example describes the identification of several fragments encoded by SEQ ID NO: 110 that are "effective for stimulating" T cells. Specifically, the response recites a list of several "positive fragments" that "were identified as being capable of stimulating proliferation of the P501S-specific T cells." With further regard to the "minimal 9-mer amino acid"

encoded by SEQ ID NO: 110 that was demonstrated as giving a "strong response" in Example 12, the response argues that this fragments as well as "larger fragments comprising " it "were shown to be capable of stimulating human T-cells." These arguments have been thoroughly considered but are not persuasive. It is again noted that the claims as written require only a step of "contacting" with "T cells," not a step, e.g., of contacting with previously stimulated T cells that are specific for P501S, as is exemplified in Example 12. The Example describes the screening of a very specific, particular type of T cell (T cells already stimulated by P501S) to determine which fragments of P501S are reactive with such T cells (and which therefore constitute reactive epitopes of the protein). While Applicants' arguments might be persuasive with respect to claims to a method such as that performed in Example 12, they are not persuasive with regard to the invention of the instant claims. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

The response further argues that, in addition to the particular fragments set forth in Example 12, "additional illustrative fragments encompassed by the claimed invention can be identified by the skilled artisan using only Applicants' disclosure in conjunction with routine methodologies described in the specification and/or available in the art." While acknowledging that "some experimentation may be required in order to identify further P501S T cell-stimulating fragments for use in the claimed methods," the response urges that such experiment would merely be routine. In response, it is acknowledged that the teachings of the specification are sufficient to enable one of skill

in the art to identify additional fragments that would be capable of stimulating the particular type of (P501S specific) T cells employed in Applicants' example 12. However, it is again noted that the instant claims are not limited to this one, specific type of cell – rather, the claims encompass the use of any type of T cells. Thus, this argument is not persuasive – as discussed above, the P501S-specific T cells of the specification possess particular properties that predispose them to react with peptides and polypeptides comprising SEQ ID NO: 337, and are clearly not representative of all "T cells."

Finally, the response argues that the specification enables the claims with regard to both the stimulation and expansion of "antigen-specific T cells," and notes that Applicants are unclear as to why "the Examiner appears to suggest that the present disclosure enables only a method in which a polypeptide of the invention is contacted with T cells which have already been stimulated, but does not enable a method in which a polypeptide of the invention is contacted with previously stimulated T cells, when it would be understood by the skilled individual that the very same P501S polypeptides useful for stimulation are also useful for expansion, and vice versa." In response, it is noted that the examiner has in fact stated that the specification is enabling of methods in which "a polypeptide of the invention is contacted with previously stimulated T cells." However, the instant claims are not limited to "previously stimulated T cells," to "antigen-specific T cells," or to, e.g., populations comprising or including such cells – rather, the claims as written merely recite "T cells." It is again noted that while the claims are

interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

7. Upon further consideration and in view of Applicants' arguments that their claim language "does not and should not limit the types of T cells employed in the claimed methods," the prior rejection of claims 35-36 and 62-66 under 35 U.S.C. 112, second paragraph, as being indefinite is withdrawn. It is clear that the claimed methods encompass the use of any type of "T cells" in the "contacting" step.

***Conclusion***

8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Diana B. Johannsen whose telephone number is 571/272-0744. The examiner can normally be reached on Monday and Thursday, 7:30 am-4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached at 571/272-0745. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Diana B. Johannsen
Primary Examiner
Art Unit 1634

2/18/06